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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/813,383	03/30/2004	Robert A. Davey	D6484	5461

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EXAMINER	
FOLEY, SHANON A	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 11/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/813,383	DAVEY ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *36-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group VIII in the reply filed on July 25, 2005 is acknowledged. Claims 36-40 are pending and under consideration.

Double Patenting

Claim 36 of this application conflict with claims 1, 8 and 9 of Application No. 1/036,568. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 36 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 8 and 9 of copending Application No. 11/036,568. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 8 and 9 of '568 are drawn to screening for a compound that

inhibits virus binding and entry into a target cell with a virus particle comprising an envelope-enzyme fusion protein and measuring the level of enzyme in infected cells. This concept is identical to the instant concept of claim 36 under examination.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 36 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dulbecco (US 4,593,002) or Young et al. (US 5,916,563). Either reference in further view of Blumenthal et al. (Journal of Biological Chemistry; 1987; 262 (28): 13614-13619).

The claims are drawn to a method of screening for a compound that inhibits the virus binding and entry into target cells by generating viruses with wild-type envelope proteins and hybrid viral envelope proteins with an enzyme fused to the C-terminal end, infecting target cells with the recombinant particles in the presence and absence of a compound and measuring activities of the enzyme in infected cells. Decreased enzyme activity indicates viral inhibition. Claim 39 lists viruses that the wild-type viral envelope protein is derived from and claim 40 states that the measurement is performed in 96-well plates.

Dulbecco teaches viruses with wild-type and chimeric envelope/capsid proteins expressed on their surfaces. Presence of the chimeric envelope proteins do not effect

reproductive abilities of the viruses, see column 2, lines 50-54, column 3, lines 54-68, column 6, lines 35-44, column 8, lines 13-17, column 11, lines 40-50 and claims 1-7. In addition, Dulbecco suggests incorporating proteins into the envelope fusion that have enzymatic activity, see column 7, lines 51-59.

Alternatively, Young et al. teach a parvovirus with wild-type VP2 capsid proteins and chimeric VP1 proteins fused with an enzyme, see column 2, lines 18-20, column 5, lines 18-37, column 7, line 58 to column 8, line 52 and claims 1-3, 6 and 7.

Neither Dulbecco nor Young et al. teach using the heterologous enzyme tag as a detection agent to screen compounds that inhibit virus binding.

However, Blumenthal et al. teach vesicular stomatitis virus with envelope proteins labeled with an octadecyl rhodamine (R18) fluorescent probe, see "Labeling of VSV with R18" bridging pages 13614-13615. Blumenthal et al. measure the amount of signal generated by the fluorescent probe on the virus in the presence of competitor molecules (unlabeled VSV, specific chemical inhibitors and neutralizing antibodies) and correlate the measurement with the quantity of labeled virus that attaches to target cells, see "Inhibition of Unlabeled VSV" on page 13616 to the second paragraph on page 13617, Figure 1b, Table 1 and Figure 2.

One of ordinary skill in the art at the time the invention was made would have been motivated to use the heterologous enzyme fused to the envelope of Dulbecco or Young et al. as an indicator to measure virus-cell fusion in the presence of inhibitors, as evidenced by Blumenthal et al. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of using the heterologous enzyme of Dulbecco or Young et al. to quantify virus-cell attachment in the presence of candidate inhibitors because the heterologous

enzyme of Dulbecco or Young et al. does not interfere with viral propagation or native viral tropism, see claims 2-4 (for example) of Dulbecco or column 5, lines 29-35 of Young et al.

Alternatively, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to fuse a detectable enzyme to an envelope protein, as taught by Dulbecco or Young et al., on surface of the VSV of Blumenthal et al. with a reasonable expectation of success since the fluorescent probe of Blumenthal et al. is inserted into the viral bilayer, see "Labeling of VSV with R18" bridging pages 13614-13615.

Claims 36, 38 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Russel et al. (WO 94/06920) and Blumenthal et al. supra.

See the summary of claims 36 and 39 above. Claims 38 and 39 require that the envelope-enzyme fusion and wild-type viral envelope protein are derived from the murine leukemia virus.

Russel et al. teach a murine leukemia virus comprising an envelope fusion with a heterologous protein, such as a functional enzyme, see the second paragraph on page 11, the paragraph bridging pages 35-36, section "7" on page 38 and claims 1-4, 6 and 7.

The teachings of Blumenthal et al. are incorporated herein.

One of ordinary skill in the art at the time the invention was made would have been motivated to use the heterologous enzyme fused to the envelope of Russel et al. as an indicator to measure virus-cell fusion in the presence of inhibitors, as evidenced by Blumenthal et al. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of using the heterologous enzyme of Russel et al. to quantify virus-cell attachment in the presence of candidate inhibitors because the heterologous enzyme of Russel et al. does not

interfere with viral propagation or native viral tropism, see the abstract and claims 4 and 7 for example.

Alternatively, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to fuse an enzyme to an envelope protein, as taught by Russel et al., on surface of the VSV of Blumenthal et al. with a reasonable expectation of success since the fluorescent probe of Blumenthal et al. is inserted into the viral bilayer, see "Labeling of VSV with R18" bridging pages 13614-13615.

Claims 37 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dulbecco or Young et al., either in view of Blumenthal et al. as applied to claims 36 and 39 above, or Russel et al. and Blumenthal as applied to claims 36, 38 and 39 above, and further in view of Goldsmith et al. (US 6,451,598 B1).

Claim 37 requires that the recombinant enzyme portion of the fusion protein is luciferase and claim 40 requires that the measurement of enzyme activity is performed in 96-well plates.

While Russel et al. teach detection of the fusion protein in 96-well plates, see "ELISA..." on page 46, none of the references cited teach fusing luciferase or measuring enzyme activity in 96-well plates.

Goldsmith et al. describe a cell fusion assay that uses luciferase as a reporter enzyme to indicate whether virus-cell fusion occurs in the presence of a candidate inhibitor, see the abstract, column 2, line 13 to column 5, line 29, column 8, lines 1-42 and claims 1-16.

In the cell fusion assay of Goldsmith et al., the first cell is analogous to the virus expressing native and envelope-enzyme fusion proteins of Dulbecco or Young et al. or Russel et al. Therefore, the express use of luciferase to quantify virus-cell fusions in the presence of

candidate inhibitor compounds would have been an obvious selection for use as the fused detectable enzyme of Dulbecco or Young et al. or Russel et al. in view of Blumenthal et al.

Although none of the references teach assaying the enzymatic activity in 96-well plates, the ordinary artisan would have been motivated to use this type of plate in order to screen as many as 94 candidate inhibitors (and comparing the enzyme activities observed with positive and negative control samples). Conventional luminometers in the art accommodate this type of platform to quantify luciferase enzyme activity.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon A. Foley whose telephone number is 2-0898. The examiner can normally be reached on 6:00 AM - 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 2-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shanon A. Foley
Primary Examiner
Art Unit 1648